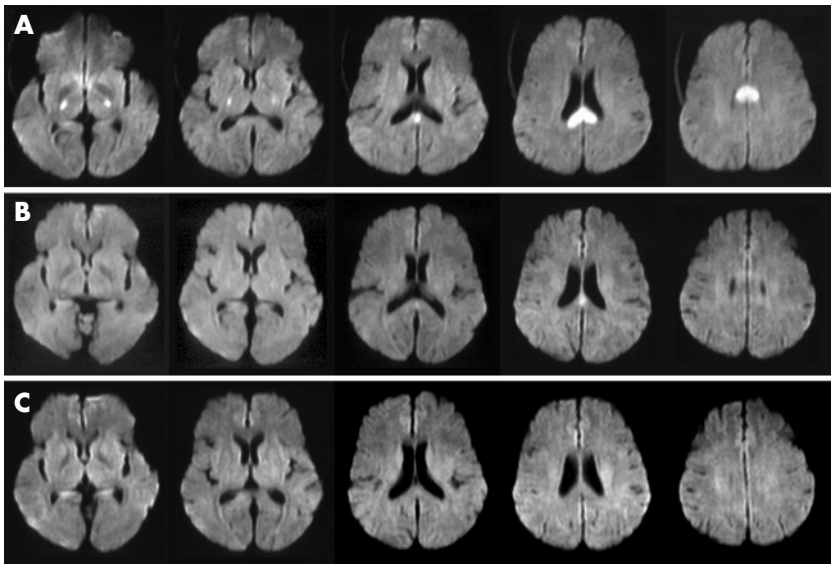

Figure 1 (A) Diffusion-weighted imaging (DWI) on admission showing hyperintense lesions in the splenium of the corpus callosum and the bilateral posterior limbs of the internal capsules. (B) DWI obtained 2 h after glucose infusion showing almost full recovery except for a small part of the splenium of the corpus callosum. (C) DWI obtained 2 days after glucose infusion showing complete regression of the hyperintense lesions.

In previously reported cases, several marked MRI findings were shown. DWI and ADC were more sensitive than fluid-attenuated inversion recovery imaging to detect the abnormal lesions.[2 3] The initial ADC values were moderately decreased, but were fully reversible.[2 3] Perfusion-weighted MRI showed no perfusion deficit[2] or a slight increase in relative cerebral blood volume restricted to the lesion seen on DWI.[3] Magnetic resonance angiography detected no haemodynamically relevant stenosis or vasospasm.[1–3] DWI showed changes localised in the splenium,[2] the internal capsule[1 3] and the corona radiata.[1 2] In our patient, the lesions were located in the splenium and the internal capsule.

Typical lesions in more severely affected patients had different localisations including the basal ganglia, the pons, the temporal and occipital cortices, and the hippocampus. Magnetic resonance signal changes in the splenium have been found in various pathological conditions such as alcohol use, infections, hypoglycaemia, trauma, salt abnormalities and seizure.[5] DWI often showed other areas of involvement, particularly the posterior limb of the internal capsule.[5] T2-relaxation MRI studies of healthy patients showed heterogeneous water content in the splenium and the posterior limbs of the internal capsule, but tissue myelin water content was relatively higher.[6] Effects associated with the splenium and the posterior limb of the internal capsule injury as described above can compromise cellular fluid regulation.[5] Our findings may support the hypothesis that the splenium and the posterior limb of the internal capsule can more easily affect cellular fluid mechanics compared with the surrounding tissue in some pathological conditions.[5]

In conclusion, abnormal hyperintense lesions on DWI in hypoglycaemic coma may disappear rapidly after glucose infusion.

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Familial Creutzfeldt–Jakob disease with E200K mutation presenting with neurosensorial hypoacusis

Creutzfeldt–Jakob disease (CJD) is characterised by rapidly progressive dementia, myoclonus, ataxia, visual disturbances and motor dysfunction. Neuropathological examination shows diffuse spongiosis, neuronal loss, gliosis and a variable degree of amyloid plaque deposition composed of protease-resistant prionic protein (PrP^{RES}) in several locations, including the brain stem. The most frequent clinical presentations are dementia, ataxia or visual symptoms. Most of the cases are sporadic. Only 10–15% are familial, and the most frequent point mutation is E200K. The course of disease, investigation results and neuropathology are similar to those of the sporadic form of CJD. The typical clinical presentation of E200K is a rapidly progressive dementia with myoclonus and pyramidal, cerebellar or extrapyramidal signs.[1] We report a familial case with an unusual onset, with deafness and polyneuropathy.

A 53-year-old man presented with subacute progressive bilateral hypoacusis, with tinnitus in the left ear. He was a frequent diver and the symptoms were attributed to barotrauma. During the following months, his hypoacusis worsened and he progressively developed bilateral stocking-type paresthaesia and gait instability. On examination, he was alert and cooperative, although communication was mildly affected because of the hypoacusis. He showed emotional lability; his speech was slow but fluent, and he was partially disoriented in time. Extrinsic ocular motility, cranial nerves and muscular strength were normal. Lower limbs showed mild hypertonia, right extensor plantar response, stocking-type hypoaesthaesia and hypopallaesthaesia, and moderate gait ataxia. An audiometric examination showed bilateral neurosensorial hypoacusis, and nerve conduction studies showed a mixed axonal polyneuropathy. Computed tomography and magnetic resonance imaging of the brain were normal and the electroencephalography (EEG) showed non-specific changes.

These symptoms led to an initial suspicion of a paraneoplastic disorder, and an examination for malignant disease was started. At this moment, we learnt that the patient's mother had died of neuropathologically confirmed CJD; hence we conducted a CSF 14-3-3-protein detection test, which was positive. Serial EEGs showed repeated non-specific changes. Brain stem auditory evoked potentials (BAEPs) could not be performed, owing to lack of patient collaboration.

During the following 2 weeks, myoclonus appeared and rapidly generalised, mental status deteriorated and progressive ataxia confined the patient to bed. He died of respiratory infection 10 months after onset of symptoms.

Neuropathological examination showed neuronal loss, microspongiosis and astroglial and microglial proliferation predominantly in the isocortex, entorhinal cortex, and hippocampal CA1 region, striatum, amygdala and cerebellar cortex. Punctate, synaptic-like deposits of PrP^{RES} in the cerebral and cerebellar cortices were found, as well as scattered large PrP^{RES} deposits in the granular layer of the cerebellum. The mesencephalon did not show spongiosis, but gliosis in colliculum and periaqueductal grey matter were detected.

Marked neuronal loss and gliosis in the vestibular and cochlear nuclei were observed, associated with PrP^{RES} deposition (fig 1). Western blot of PrP^{RES} showed a three-band pattern, with an unglycated fragment migrating at 21 kDa, corresponding to PrP^{RES} type 1. Genetic sequencing of PrP showed the presence of the E200K mutation in heterozygosis. No insertions or deletions were found in the 51–91 region. The patient was heterozygotic for the M/V polymorphism at codon 129.

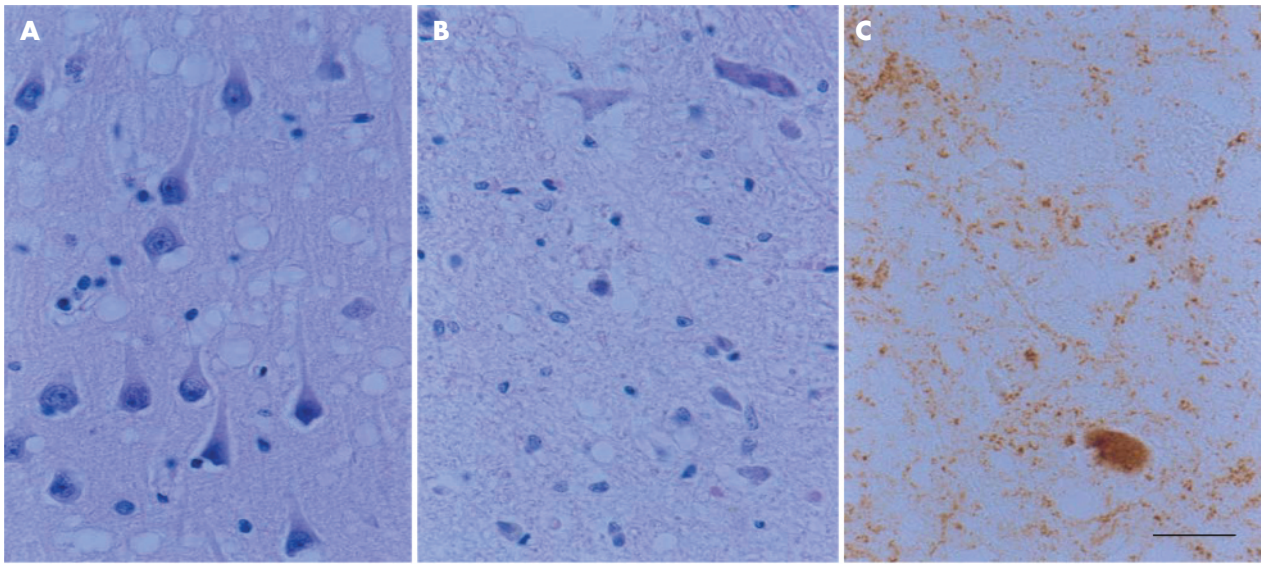

Figure 1 (A) Frontal cortex with moderate neurone loss, neuronal vacuoles and spongiform change. (B) Ventral cochlear nucleus showing the almost absence of large neurones. (C) Punctate PrPres immunostaining in the lateral vestibular nucleus. Paraffin sections (A,B) Haematoxylin and eosin staining; c:PrP^{RES} immunohistochemistry. Scale bar = 25 μm.

Only two cases of CJD with deafness at onset have been published: one sporadic, associated with symptoms suggestive of polyneuropathy,[2] and the other familial, with the E200K mutation and typical features.[3] Other cases have been reported as presenting with auditory agnosia or with cortical deafness, and early involvement of the acoustic pathway was already detected through demonstration of progressive BAEP deterioration in patients with CJD who did not present deafness in the course of the disease.

The first case was that of a 71-year-old woman who presented with a sudden change in hearing and aural fullness, and a vague feeling of imbalance.[2] Hearing loss and gait instability worsened rapidly Audiometry showed bilateral neurosensorial hearing loss, and BAEPs were initially normal. She later developed signs of polyneuropathy and mental deterioration, left homonynous hemianopsia and decreased vibratory and pinprick sensation. The second case was that of a 46-year-old Italian woman with the E200K mutation, who had rapidly worsening hearing loss.[3] Three weeks later she developed an unstable gait, and her condition rapidly progressed to bilateral deafness, ataxia, myoclonus, pyramidal and extrapyramidal dysfunction, and mental deterioration. She died 6 months after the onset of the disease. Magnetic resonance imaging scans showed high signal areas, mostly in the caudate and putamen, EEGs showed periodic sharp-wave complexes, and protein 14-3-3 was present in the cerebrospinal fluid. Audiometric investigation showed bilateral sensorineural hearing loss, and BAEP abnormalities from the beginning seemed to confirm early brain stem involvement. The course of the illness, clinical features and EEG recordings were similar to those of the sporadic form of CJD.

Accumulation of PrP in the brain stem has been found to be an early pathological event in sporadic CJD, but these deposits are not necessarily associated with clinical symptoms or neuronal loss, and the brain stem seems to remain relatively resistant to the pathological process of sporadic CJD.[4] Neuropathological changes in brain stem structures have been described in sporadic and familial CJD, associated with atypical onset, with gaze disorders and with fatal familial insomnia. Unfortunately, necropsy was not possible in the two patients with early deafness, and to our knowledge specific involvement of cochlear and vestibular nuclei has not been reported previously

Western blot of PrP showed a type 1 pattern in our case. This is the pattern usually observed in sporadic CJD M/M homozygotic at codon 129, and it has also been described in patients with the E200K mutation associated with the allele 129M in the mutated chromosome.[5] It is not known whether the glycation pattern of abnormal PrP has an influence on phenotype. In our patient also, who was M/V homozygotic, the codon 129 status of the mutated allele was not investigated.

This case illustrates the phenotypic variability of presentation of CJD, and describes the specific involvement of brain stem auditive nuclei in a patient with hypoacusis as the initial manifestation, thereby reflecting early brain stem involvement.

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Fugue associated with migraine

Case history

A 33-year-old man was brought by ambulance to the emergency department from a local park with a right-sided headache and amnesia. He did not know his name, age, address, occupation or marital status. He could not remember how he came to be in the park, nor could he recall any autobiographical event before that morning. Despite this alarming deficit, he responded to all questions directly, showing surprisingly little distress at his predicament. Cognitive testing showed that he was orientated to time and place, and able to perform well on tests of attention, concentration and recall. He was afebrile, and his physical examination was unremarkable. We observed no signs of head trauma or substance intoxication or withdrawal. His blood alcohol